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Predictors of In-Hospital Mortality after Recovered Out-of-Hospital Cardiac Arrest in Patients with Proven Significant Coronary Artery Disease: A Retrospective Study

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Abstract

Introduction: Recovered Out-of-Hospital Cardiac Arrest (rOHCA) population is heterogenous. Few studies focused on outcomes in the rOHCA subgroup with proven significant coronary artery disease (SigCAD). We aimed to characterize this subgroup and study the determinants of in-hospital mortality. **Methods**: Retrospective study of consecutive rOHCA patients submitted to coronary angiography. Only patients with SigCAD were included. **Results**: 60 patients were studied, 85% were male, mean age was 62.6 ± 12.1 years. In-hospital mortality rate was 43.3%. Patients with diabetes and history of stroke were less likely to survive. Significant univariate predictors of in-hospital mortality were further analysed separately, according to whether they were present at hospital admission or developed during hospital evolution. At hospital admission, initial non-shockable rhythm, low-flow time>12min, pH<7.25mmol/L and lactates >4.75mmol/L were the most relevant predictors and therefore included in a score tested by Kaplan-Meyer. Patients who had 0/4 criteria had 100% chance of survival till hospital discharge, 1/4 had 77%, 2/4 had 50%, 3/4 had 25%. Patients with all 4 criteria had 0% survival. During in-hospital evolution, a pH<7.35 at 24h, lactates>2mmol/L at 24h, anoxic brain injury and persistent hemodynamic instability proved significant. Patients who had 0/4 of these in-hospital criteria had 100% chance of survival till hospital discharge, 1/4 had 94%, 2/4 had 47%, 3/4 had 25%. Patients with all 4 criteria had 0% survival. Contrarily, CAD severity and ventricular dysfunction didn't significantly correlate to the outcome. **Conclusion**: Classic prehospital variables retain their value in predicting mortality in the specific group of OHCA with SigCAD. In-hospital evolution variables proved to add value in mortality prediction. Combining these simple variables in risk scores might help refining prognostic prediction in these patients's subset.

Keywords: out-of-hospital cardiac arrest, return of spontaneous circulation, coronary artery disease, coronary angiography, in-hospital mortality

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Introduction

Out-of-Hospital Cardiac Arrest (OHCA) remains one of the most challenging health care problems, despite recent efforts to improve cardiopulmonary resuscitation (CPR) with the development of evidence-based guidelines and care-bundle systems. The number of patients who achieve return of spontaneous circulation (ROSC) and survive to hospital discharge varies from 7 to 40% depending on the clinical setting [1-6]. The bulk of the available data reporting survival predictors, comes from studies addressing the overall OHCA population, regardless of the cause of the arrest. As a consequence, different epidemiological and pathophysiological features are usually included in the same analysis. Trying to extrapolate information from these data to predict in-hospital mortality within specific etiologic OHCA subgroups can be challenging. Furthermore, predicting cause of death by clinical presentation and risk factors is difficult. A recent prospective study

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performed autopsies on 896 patients with a presumed cardiac cause for the arrest [7]. The investigators concluded that in 40% of cases the death was not of primary cardiac origin as initially thought.

Coronary Artery Disease (CAD) is considered the main cause of OHCA in adults. Based on studies performed in the first decade of the millennium, the American Heart Association scientific statement reports that up to 70% of OHCA patients have CAD with 50% having an acute plaque event [8].

Multiple studies have explored the predictors of CAD and survival in the global OHCA population [9-11]. However, in the specific subgroup of rOHCA patients with proven significant SigCAD, consistent data regarding to their specific clinical, biochemical and imaging prognostic features is still scarce. Our goal was to establish predictors of in-hospital in a series of rOHCA-patients with SigCAD.

Methods

Retrospective observational study of consecutive patients admitted after rOHCA and submitted to coronary angiography (CA) in the subsequent 48 hours. The study was conducted at Centro Hospitalar Universitário do Porto, from October 2006 to July 2018. It was approved by the Hospital's Ethic Committee (approval code: 237-18 - 207-DEFI/206-CES). The decision to perform CA was based on the clinical probability of acute coronary syndrome. Immediate CA was performed in OHCA patients presenting with ST-segment elevation. For other OHCA patients of suspected coronary cause, the timing was decided after multidisciplinary discussion including cardiology and intensive care specialists. In accordance with revascularisation guidelines [12], SigCAD was defined as >70% stenosis in the major epicardial vessels or >50% in left main and/or need for percutaneous coronary intervention [13, 14], and was used to indicate CAD as the cause of OHCA.

Echocardiography was performed by experienced cardiologists. Left ventricular ejection fraction (LVEF) was assessed by Simpson's Biplane method. It was considered midly abnormal if LVEF was between 41-51%, moderately abnormal if LVEF was 30-40% and severely abnormal if LVEF was bellow 30%.

Persistent hemodynamic instability was defined as the need for vasopressor or inotropic support to maintain organ perfusion beyond 24h after admission and/or recurrent severe arrythmias. The diagnostis of anoxic brain injury was made after proper assessment and testing by a neurologist.

In-hospital variables, demographic and clinical characteristics and in-hospital evolution data, including diagnostic tests, therapeutic options and cardiovascular status were analysed by chart review. Collected data was anonymised.

Descriptive statistics were summarized as percentages for categorical variables and as mean ± standard deviation or median ± interquartile range for continuous variables. We used: logarithmic transformation of skewed data to enable utilization of parametric tests; Pearson X^2 test and Student's t-test to identify variables associated with in-hospital mortality. Best cut-off points of continuous variables were determined using receiver-operator (ROC) curves analysis. Variables with $p<0.05$ by univariate analysis entered a logistic regression equation to characterize independent predictors for mortality. In multivariate regression and in Kaplan-Meier survival analysis significant variables were analysed separetely according to their time of appearance: present at hospital admission or developed during in-hospital evolution. These method was used to facilitate interpretation of data and clinical applicability.

All statistical analyses were performed using IBM SPSS Statistics for Windows (Version 25.0. Armonk, NY: IBM Corp)

Results

The initial study population consisted of 73 rOHCA that underwent CA. Among them, 10 didn't have CAD and 3 didn't have angiographically SigCAD and were therefore excluded from the analysis. 60 patients with rOHCA and proven CAD were included in this study.

Clinical and demographic characteristics are presented in table 1. Patients were mainly male (85%) with a mean age of 62.6±12.1 years-old. Regarding to cardiovascular risk factors, 54% of patients were hypertensive, 25% were diabetic (type 2), 57% had dyslipidaemia, 58% were or had been smokers and 15% were obese. 38% of patients had a known history of CAD and 5% had cerebrovascular disease.

Cardiac arrest happened most commonly in a public place (45% of cases), at home in 22%, during the transport to the hospital in 5.0% and at the hospital premises but before observation by health staff in 28% of cases. The median low-flow time [time from the beginning

Table 1 - Baseline and clinical characteristics

	Overall n=60	Group 1 rOHCA non-survivors n=26 (43.3%)	Group 2 rOHCA survivors n=34 (56.7%)	P value
Patients clinical profile				
Age in years, mean (std dev)	62.6 ± 12.1	65.5 ± 10.6	60.3 ± 12.8	0.1
Gender, male	51 (85.0%)	22 (84.6%)	29 (85.3%)	0.9
CV risk factors				
Hypertension	35 (58.3%)	18 (69.2%)	17 (50.0%)	0.1
Smoking	35 (58.3%)	12 (46.2%)	23 (67.6%)	0.1
Dyslipidemia	34 (56.7%)	15 (57.7%)	19 (55.9%)	0.9
previous Coronary Artery Disease	23 (38.3%)	12 (46.2%)	11 (32.4%)	0.3
Previous myocardial Infarction	19 (31.7%)	7 (26.9%)	12 (35.3%)	0.5
Diabetes	15 (25.0%)	11 (42.3%)	4 (11.8%)	0.007
Heart Failure	11 (18.3%)	6 (23.1%)	5 (14.7%)	0.4
pPCI	10 (16.7%)	4 (15.4%)	6 (17.6%)	0.8
Peripheral vascular disease	10 (16.7%)	6 (23.1%)	4 (11.8%)	0.2
Obesity	9 (15.0%)	4 (15.4%)	5 (14.7%)	0.9
pCABG	7 (11.7%)	3 (11.5%)	4 (11.8%)	1.0
COPD	4 (6.7%)	2 (7.7%)	2 (5.9%)	0.8
Stroke	3 (5.0%)	3 (11.5%)	0 (0.0%)	0.042
Pre-hospital variables				
Means of transport				
Medical emergency team	39 (65.0%)	20 (76.9%)	19 (55.9%)	0.1
Location of cardiac arrest				0.002
Public/Private setting	40 (66.7%)	23 (88.5%)	17 (50%)	
Hospital premises/Transport	20 (33.3%)	3 (11.5%)	17 (50%)	
Time from BLS to ROSC, minutes¥ (std dev)	17±13.1	22.1±11.4	13.3±2	0.001
Adrenaline pre-ROSC, mg¥ (std dev)	2.6 ± 2.8	3.6 ± 3.0	1.8 ± 2.3	0.009#
New Cardiac Arrest	14 (23.3%)	8 (30.3%)	6 (17.6%)	0.2
Initial arrest rhythm				0.002
VT/VF	46 (76.7%)	15 (57.7%)	31 (91.2%)	
PEA/asystole	14 (23.3%)	11 (42.3%)	3 (8.8%)	
Chest pain	24 (40.0%)	7 (26.9%)	17 (50.0%)	0.1
First EKG				
STEMI	36 (60.0%)	15 (57.7%)	21 (61.8%)	0.8

rOHCA- recovered Out of Hospital Cardiac Arrest; CAD - Coronary Artery Disease; pPCI – previous percutaneous coronary intervention; PVD – Peripheral Vascular Disease; pCABG – previous Coronary Artery Bypass Graft; COPD – Chronic Obstructive Pulmonary Disease; VMER – Medical Emergency and Reanimation Vehicle; BLS – Basic Life Support; ROSC – Return Of Spontaneous Circulation; VT – Ventricular Tachycardia; VF – Ventricular Fibrillation; PEA – Pulseless Electrical Activity; EKG – Electrocardiogram; STEMI – ST-elevation myocardial infarction; NSTEMI – Non ST-elevation myocardial infarction; std dev- standard deviation; ¥- 1 missing in group 1; # - Mann-Whitney test

of basic life support (BLS) manoeuvres to ROSC] was 12±13 minutes. During advanced life support (ALS) manoeuvres, the mean dose of adrenaline administered was 2.6 ± 2.8 mg. Most patients presented with a shockable initial rhythm (77%). Chest pain was present before arrest in 40% of the patients. On the post-ROSC electrocardiogram, an ST-segment elevation pattern was identified in 60% cases.

In coronary angiography, the majority of patients (90%) had at least 1 critical to suboclusive lesion (70-90% angiographically-estimated stenosis) and 73% had an acute segment occlusion. 63% of patients had multivessel disease and 22% had significant stenosis in the left main or proximal left anterior descending artery. 72% of patients underwent percutaneous coronary intervention (PCI), 95% of which had culprit-lesion only PCI. There's was PCI failure in 7% of cases. Echocardiographic data was available for 95% of patients. A moderate to severe left ventricle dysfunction was present in 67% of patients assessed in the first 24 hours. No other relevant features beside LVEF were found.

Predictors of in-hospital mortality

In-Hospital mortality was 43.3%. Age and gender differences didn't influence mortality. rOHCA non-survivors had a higher incidence of diabetes (42.3% vs 11.8%, p=0.01) and cerebrovascular disease (11.5% vs 0%, p=0.042). Diabetes also associated with a higher likelihood of multivessel disease (53% vs 93%, p=0.02, OR 12). With respect to other classic cardiovascular risk factors, no differences between groups were found (Table 1).

Regarding to pre-hospital variables (Table 1), rOHCA non-survivors were more likely to present with a non-shockable initial arrest rhythm (43.3% vs 8.8%, OR 7.5, p= 0.005), a longer low-flow time (17±13 min vs 22±11min, OR 3.3, p=0.003) and to be administered higher doses of adrenaline during ALS (3.6±3.0mg vs 1.8±2.3mg, OR 1.31 p=0.017). The best cut-off of low-flow time to predict survival was 11.5 min [area under the curve (AUC) by ROC analysis: 0.75] .

There was no statistically significant difference in outcome related to the presence of ST-elevation, the extent of CAD and revascularisation strategy. However, non-survivors had a higher incidence of multivessel disease, larger troponin elevations and were less likely to receive PCI (Table 2).

The presence of moderate to severe left ventricular dysfunction, at hospital admission or during follow-up, didn't influence mortality (Table 2).

Lactate levels in blood-gas analysis were higher in non-survivors: 7.9±5.1 vs 5.4±4.7mmol/L, OR 1.9, p=0.045. Non-survivors also had a lower lactate clearance in serial testing during the first 6 hours: 3.9±3.7 vs 2.2±1.5mmol/L, OR 2.2, p=0.048. Lower pH level at admission (7.17 ± 0.18 vs 7.27 ± 0.19, OR 0.05, p=0.046) was linked to the outcome. Reevaluation performed ~24h after admission revealed that the persistence of values out of the normal reference for pH and lactate (pH<7.35, OR 4.9, p=0.01 and lactates >2mmol/L, OR 3.4, p=0.04) signalled mortality (Table 3). The best cut-off point for lactate and pH at admission defined by ROC curve was 4.95mmol/L (AUC 0.65) and 7.25 (AUC 0.70), respectively.

In-hospital evolution in non-survivors was associated with serious complications (Table 2). rOHCA non-survivors had a significantly higher incidence of anoxic brain injury (57.7% vs 23.5%, p=0.007) and persistent hemodynamic instability (96% vs 38%, OR 4,4, p=0.001). As expected, the median duration of hospital stay was longer in the rOHCA survivors' group (15, 6-22 days vs 3, 2-6 days, p<0.001).

In multivariate analysis of variables present at hospital admission, low-flow time superior to 12 minutes (p=0.006, OR 10.9) and non-shockable rhytmn (p=0.02, OR 6.9) independently predicted death. In multivariate analysis of in-hospital evolution variables, persistent hemodynamic instability independently associated with death (p=0.009, OR 24) (Table 4).

Table 2 - Imaging and in-hospital complications data

	Group 1 rOHCA non-survivors n=26 (43.3%)	Group 2 rOHCA survivors n=34 (56.7%)	P value
Cardiac Catheterization			
Multivessel Disease	20 (76.9%)	18 (52.9%)	0.06
Left main disease or anterior descending artery	3 (11.5%)	10 (29.4%)	0.09
Percutaneous coronary intervention	17 (65.4%)	26 (76.5%)	0.3
Failure	1 (5.9%)	2 (7.7%)	0.8
Complete revascularization	2 (11.8%)	0 (0.0%)	0.2*
Echocardiogram			
Left ventricle disfunction moderate/severe			
admission¥¥	17 (73.9%)	23 (67.6%)	0.6
in-hospital evaluation¥¥¥	14 (70%)	22 (64.7%)	0.7
In-hospital complications			
Persistent hemodynamic instability	25 (96.2%)	13 (38.2%)	<0.001
Anoxic brain injury	15 (57.7%)	8 (23.5%)	0.007
Median duration of stay, days (IQR)	3 (2-6)	15 (6-22)	<0.001#
Median intensive care unit, days (IQR)	3 (2-6)	6 (4-12)	0.1#

*- Fisher's exact test; # - Median test; ¥¥- 3 missing in group 1; ¥¥¥-6 missing in group1

Table 3. Clinical scores and biochemical data

	Group 1 rOHCA non-survivors n=26 (43.3%)	Group 2 rOHCA survivors n=34 (56.7%)	P value
Clinical scores			
GRACE score (mean, std dev)			
admission¥	174.8 ± 37.8	160.8 ± 32.1	0.1#
24-48h¥/µ	176.2 ± 33.4	151.2 ± 31.9	0.041#
Biochemical data (mean, std dev)			
Troponin T (ng/mL)*			
admission¥¥/∞∞	6.4±23	1.9±4.6	0.074
24h¥¥¥¥/∞∞	6.3±9	2.8±2.9	0.086
C-reactive protein (mg/L)**			
admission∞	15.7 ± 49.2	18.27 ± 53.2	0.6#
24h¥¥¥/∞	54.3 ± 54.4	57.5 +/- 55.7	0.7#
Creatinine (mg/dL)***			
Admission	1.36 ± 0.53	1.32 ± 0.83	0.2#
24h-48h¥¥¥	1.32 ± 0.74	1.25 ± 1.27	0.2#
Neutrophils (x10^3/µL)			
Admission	10.1±3.4	10±6.1	0.9
24-48h¥¥¥	13.5±7.4	10.2±3.6	0.1
Haemoglobin (g/L)			
Admission	13.6 ± 2.1	14.1 ± 2.0	0.2
24-48h¥¥¥	13.8 ± 2.5	13.0 ± 1.6	0.1
Lactates (mmol/L)			
admission∑	7.9±5.1	5.4±4.7	0.039
1-6h¥/∑	3.9±3.9	2.2±1.5	0.040
24-48h¥¥¥/∞∞∞∞	2.3±1.9	1.4±0.8	0.084
pH			
admission∞∞	7.17 ± 0.18	7.27 ± 0.19	0.011#
24-48h¥¥¥/∑	7.32 ± 0.10	7.41 ± 0.05	<0.001#

*Troponin T – Elecsys® (Roche®) high sensitive assay –upper reference limit (99th percentile): 0.0014 ng/mL; ** C reactive protein - range of normal values according to the specific laboratory test: 0-5mg/L; *** Creatinine – range of normal values according to the specific laboratory test: 0.7-1.2 mg/dL; # Mann-Whitney test ; std dev- standard deviation; ¥ 1 missing in group 1; ¥¥- 3 missing in group 1; µ - 5 missing in group 1 ¥¥¥- 6 missing in group 1; ¥µ-7 missing in group 1 ¥¥¥¥ - 8 missing in group 1; ∞- 1 missing in group 2; ∞∞- 3 missing in group 2; ∑- 4 missing in group 2 ;∑∑- 5 misisng in group 2; ∞∞∞∞ - 6 missing in group 2.

Survival analysis

Survival according to the number of significant high-risk variables present at hospital admission and during hospital evolution was calculated using the Kaplan–Meier method. At hospital admission, initial rhythm, low-flow time, pH and lactates were the most relevant predictors and therefore were included in the score. Patients who had 0/4 criteria had 100% chance of survival till hospital discharge, 1/4 had 77%, 2/4 had 50%, 3/4 had 25%, respectively. Patients with all 4 criteria had 0% survival (log-rank p<0.001) (Figure 1). During hospital evolution, a pH<7.35 at 24h, lactates>2mmol/L at 24h, anoxic brain injury and persistent hemodynamic instability proved significant. Patients who had 0/4 criteria had 100% chance of survival till hospital discharge, 1/4 had 94%, 2/4 had 47%, 3/4 had 25%, re-

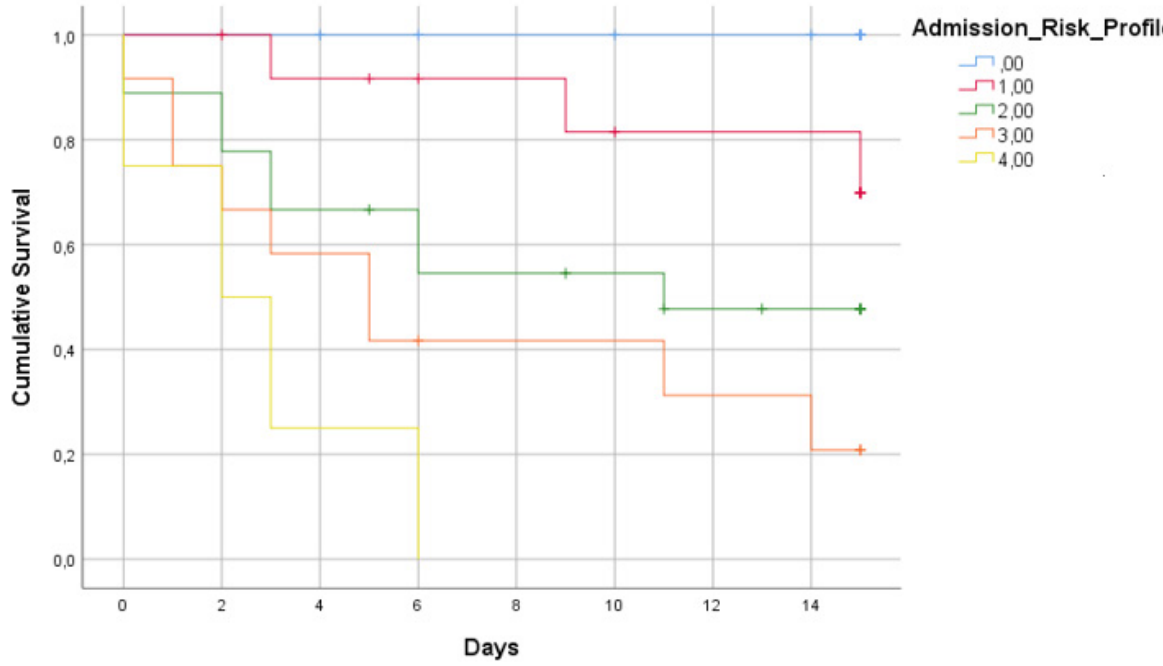

Fig. 1. Survival according to the number of significant high-risk criteria present at admission: pH <7.25 mmol/L; Lactate >4.95 mmol/L; Time to ROSC >12 min; Non-shockable initial rhythm.

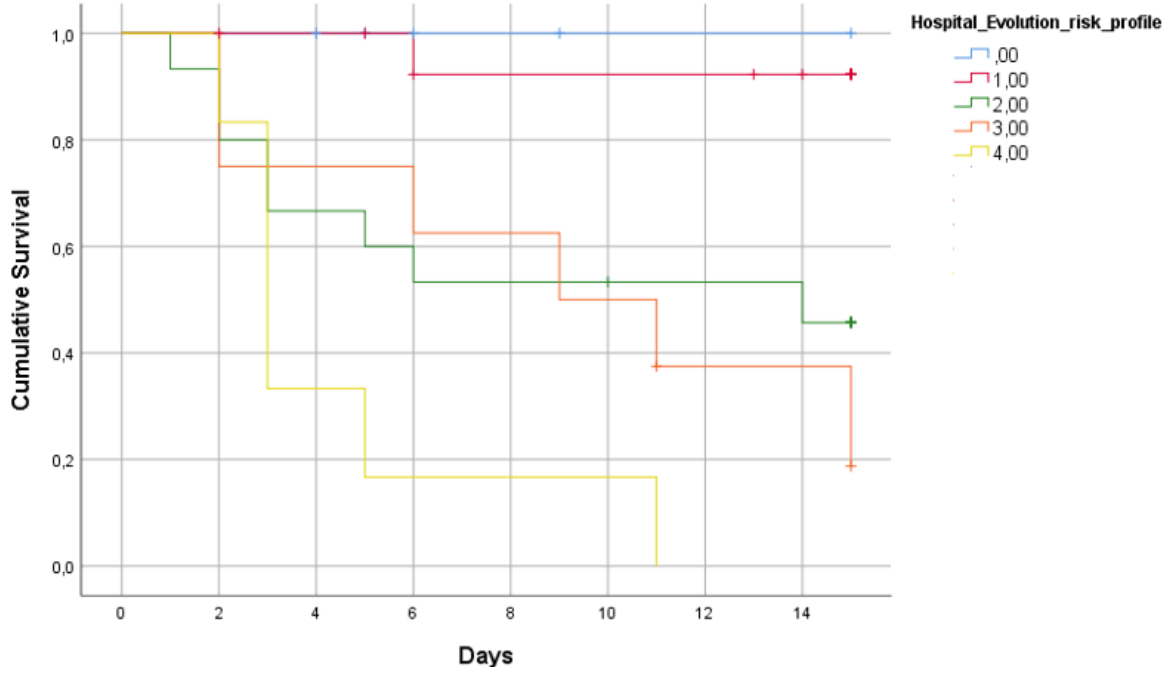

Fig. 2. Survival according to the number of significant high-risk criteria present during hospital evolution: pH <7.35 mmol/L at 24h; Lactate >2 mmol/L at 24h; anoxic brain injury; persistent hemodynamic instability

spectively. Patients with all 4 criteria had 0% survival (log-rank p<0.001)(Figure 2).

Discussion

Our real word study focused on OHCA patients with proven sigCAD. The OHCA population is quite heterogeneous but this OHCA subgroup shares a common pathophysiological mechanism leading to the arrest. By addressing only these patients we tried to improve clarity and the clinical applicability of prognostic predictors.

The main findings of this study are the following: First, we corroborate the prognostic utility of classically

Table 4 - Multivariate regression analysis

	P value	Odds Ratio
Hospital Admission Variables		
Low-flow time >12 minutes	0.006	10.9
Lactates >4.95mmol/L	0.232	2.8
pH<7.25	0.075	4.2
Non-shockable initial rhythm	0.02	6.9
In-Hospital Evolution Variables		
Anoxic brain lesion	0.056	6
Persistent hemodynamic instability	0.009	24
pH <7.35 at 24h	0.116	4.9
Lactates >2mmol/L at 24h	0.056	6.3

used predictors of mortality in OHCA patients in this specific rOHCA subgroup, and add that in-hospital variables also signal mortality. Secondly, the severity of CAD and ventricular dysfunction didn't significantly correlate to in-hospital mortality.

PreHospital Variables

Shockable initial rhythm, witnessed cardiac arrest, bystander CPR and lower low-flow time increase the likelihood of survival. Multiple studies have proven that no-flow (time between the arrest and the beginning of BLS manoeuvres) and low-flow time (time from the beginning of BLS to ROSC) together with the quality of the cardiac massage are the major determinants of the success in attaining ROSC [15-17]. Likewise, an initial shockable rhythm predicts better outcomes since an effective treatment (i.e. shock/defibrillation) is immediately available to paramedics. Interestingly, Wah et al showed that an initial non-shockable rhythm, subsequently converted to a shockable rhythm was associated with better post-arrest survival and neurological outcomes when compared to a "continuous" non-shockable rhythm [18] .

On the other hand, a non-shockable rhythm can be the initial arrest rhythm, in which case it tends to reflect a more chronic severe condition prior to the arrest and/or is the consequence of longer delays in response that increase the probability of an initial shockable rhythm turning into a non-shockable one. An arrest at home/private setting is less likely to be promptly rescued by professionals or people who can perform BLS manoeuvres. Therefore, there is a higher probability of deterioration of the patient's status. However, regardless of the circumstances and primary pathophysiologic mechanism, a non-shockable rhythm strongly correlates with worse outcomes [19].

Adrenaline is one of the few drugs incorporated in advanced life support algorithms [20]. The vasoconstriction effect is mediated by α-adrenergic receptors and promotes increased coronary blood flow, leading to increased probability of ROSC but has no impact in survival to hospital discharge [21-24]. Higher doses of adrenaline pre-ROSC associate with lower survival rate during hospital stay as they correlate directly with longer low-flow times [22, 23]. Furthermore, adrenaline was linked to ischemic lesions provoked by the vasoconstrictor effects on microvascular cerebral circulation and correlated to higher risk of poor neurological outcome [21, 25]. In the recent PARAMEDIC-2 trial >8000 patients were randomized to either adrenaline or placebo during ALS efforts. Investigators found that the use of adrenaline resulted in a higher rate of 30-day survival. However, there was no difference between the groups (adrenaline vs placebo) concerning the rate of a neurological favourable outcome since survivors in the adrenaline group had more frequently severe neurological impairment [25]. This powerful trial confirms the results of previous observational studies and questions the role of adrenaline use during OHCA.

Cardiac findings

The majority of studies refer an association between in-hospital survival and the performance of CA and PCI if necessary [1, 15, 26]. However, contrary to our study where only patients with sigCAD were included, the majority of these studies enrol patients with both coronary and non-coronary causes for OHCA. A study in OHCA patients with STEMI found that cardiogenic shock and multivessel disease were associated with mortality [9]. Our findings also revealed a tendency for more severe CAD and larger infarcts sizes (reflected by higher troponin elevations) in non-survivors although it didn't reach statistical significance, pointing to the need of larger studies to prove its impact on survival

LVEF is considered an echocardiographic measure of myocardial dysfunction but its prognostic significance in OHCA patients is controversial and robust data is missing. Some observational studies report an association between LV dysfunction and survival [27, 28] while others [3, 29, 30], like ours, found that it doesn't impact outcomes. Interestingly, Jentzer et al, showed that diastolic dysfunction is associated with in-hospital and long-term mortality, considering it a more important variable in predicting patient outcomes [31].

Metabolic alterations

Blood-gas analysis provides critical information after rOHCA and unfavourable outcomes correlate with higher lactate and lower pH levels at admission and during hospital stay, reflecting a longer body exposure to ischemia [32-34]. However, the cut-off points of blood lactate and pH levels are not well established. pH is influenced by CO2 clearance, HCO3- and anion gap which includes lactates, hence its variation may reflect more broadly on the status of vital organs. pH levels can therefore be a more specific predictor of outcome when compared to lactate levels, as seen in Momiyama et al [34]. In our study, we went further in exploring the importance of metabolic alterations. Interestingly, we found that the inability to achieve metabolic balance, expressed by the maintenance of altered values at the 24h blood-gas analysis, strongly correlated with mortality. This persistent metabolic derangements reflect circulatory failure with subsequent impaired regulation of homeostasis, both of which classically associated with dismal prognosis.

In-Hospital Evolution

In-hospital complications are frequent in OHCA patients. Anoxic brain injury is the most frequent cause of death after OHCA occurring in up to 66% of patients [35]. Current guidelines recommend using information from clinical, biochemical and imaging tests performed >72h after the arrest to more accurately define irreversible neurological damage[36]. Using this criteria, anoxic brain injury was present in 38% of our patients and powerfully signalled mortality. Accurately defining a poor neurologic outcome in the OHCA population is of crucial importance to avoid untimely withdrawal of care.

Hemodynamic instability was present in 63% of the patients included in this study and independently related to mortality. Clinically, it can manifest as persistent hypotension, low cardiac index and dysrhythmias and is a common complication of OHCA. The mechanisms leading to persistent instability include hypovolemia, microcirculatory deregulation and myocardial dysfunction [37]. Hypovolemia is common and can be caused by hypothermia-induced diuretic effect, by active blood loss or by loss of plasmatic fluid to extravascular compartments. The typical reperfusion injury after OHCA is caused by marked inflammatory response, leading to microcirculatory dysfunction and impaired regulation of vasoconstriction [38]. These mechanism not only aggravate ongoing ischemia and multiorgan dysfunction but also potentiate each other, leading to a vicious circle that might culminate in death.

Predicting survival in OHCA patients with SigCAD

The management of post-arrest patients is challenging. Although there are multiple risk-stratifying scores in this population, its use is not widespread.Limiting factors include their complexity and the lack of applicability in particular scenarios. The acute physiology and chronic health evaluation (APACHE) II score was developed in 1985 and is still one of the most widely used score in intensive care units (ICU) [39]. Although more recent versions were published, they are not freely available (under copyright control). The APACHE II score uses a range of simple demographic, clinical and biochemical variables to determine prognosis. This score was validated for the general ICU population and there are some challenges when it comes to its direct application to OHCA patients: First, it doesn't include OHCA as a variable, which is of critical importance to the patient outcome. The score applicability in post cardiac-arrest was tested in a prospective study that concluded it was a poor predictor of the outcome [40]. Second, risk estimation calculations were done in 1985 and are probably less accurate in estimating prognosis in patients treated nowadays.

The OHCA score propectively validated the use of 5 variables (shockable rhytmn, no-low time, low-flow time, creatinine and lactates) to predict mortality after OHCA [41]. In this study, logarithmic transformation of continuous variables was performed to avoid the "class jump phenomenon". The authors refer that this method contributed to the good performance of the score (AUC 0.88). However, the score is not readily available in standard online medical calculators and the need to use mathematical functions for each variable makes it less user-friendly.

Skrifvars et al. compared the performances of the APACHE III and the OHCA scores to predict outcome following OHCA. The authors concluded that both scores offer moderate predictive accuracy (AUC for OHCA score: 0.77; for APACHE III score: 0.71) but correlate weakly with each other [42].

In the present study, we first corroborated the usefulness of classical variables in this rOHCA subgroup;- Then, we tried to refine its clinical applicability. The use of the 4 hospital admission variables, namely pH, lactates, low-flow time and initial rhythm,lead to a risk of

death stratification of patients at admission. The presence of 4/4 at hospital admission estimated a 100% mortality in our series. Likewise, during in-hospital evolution, having persistent hemodynamic instability, anoxic brain injury and the inability to achieve metabolic balance clearly signalled a high mortality risk. Our simple approach might contribute to the identification of patients at high risk for adverse outcomes. However, larger studies are needed to validate this findings.

Taken together, these data reinforces the notion that a "one size fits all" score will hardly be found for OHCA. Therefore, prognostic assessment in these patients needs to be individualized.

Study limitations

We faced some challenges along our work. The retrospective nature of this study and the fact that it was based on medical records resulted in missing data to some extent, making it more prone to be influenced by bias and confounding factors. Our inclusion criteria were defined to better portray a group of patients with specific features. However, they inevitably led to a smaller sample size, that limited the study power to detect variables that may be associated with in-hospital mortality.

Conclusion

Managing OHCA patients is a great challenge involving complex decisions. Clinicians need to take into account multiple factors,namely patient related, cause related and circumstances of the arrest related, along with in-hospital evolution.

Our study demonstrates that classic prognostic variables retain their value in the specific subgroup of OHCA patients with SigCAD. By combining simple variables we were able to refine prognostic prediction in these patients. Furthermore, in patients with known SigCAD, CAD complexity and procedural aspects were not useful to determine prognosis.

Conflict of interest

None to declare.

Refernces

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